

## Abstract

Presented are ways to address the problem of replication competent adenovirus in adenoviral production for use with, for example, gene therapy. Packaging cells having no overlapping sequences with a selected vector and are suited for large scale production of recombinant adenoviruses. A system for use with the invention produces adenovirus incapable of replicating. The system includes a primary cell containing a nucleic acid based on or derived from adenovirus and an isolated recombinant nucleic acid molecule for transfer into the primary cell. The isolated recombinant nucleic acid molecule is based on or derived from an adenovirus, and further has at least one functional encapsidating signal, and at least one functional Inverted Terminal Repeat. The isolated recombinant nucleic acid molecule lacks overlapping sequences with the nucleic acid of the cell. Otherwise, the overlapping sequences would enable homologous recombination leading to replication competent adenovirus in the primary cell into which the isolated recombinant nucleic acid molecule is to be transferred.